

What is Claimed Is:

1. A chimeric HPV L1 protein capable of eliciting antibody responses or cellular responses that are generally comparable to those induced by two or more individual HPV types.
- 5 2. The chimeric HPV L1 protein of claim 1, wherein said two or more HPV types are selected from the group consisting of HPV-6, -11, -16, -18, -31, -33, -35, -39, and -45.
- 10 3. The chimeric HPV L1 protein of claim 2, wherein said HPV types are HPV-18 and HPV-45.
- 15 4. The chimeric HPV L1 protein of claim 3 comprising at least the R5 epitope of HPV-18.
5. The chimeric HPV L1 protein of claim 4 comprising at least amino acids 53-194 of HPV-18.
- 20 6. The chimeric HPV L1 protein of claim 5 comprising at least the N' terminus half (approximately amino acids 1-194) of HPV-18.
7. The chimeric L1 protein of claim 1 that comprises at least three segments, wherein segments 1 and 2 are adjacent and are derived from different HPV types, and segments 2 and 3 are adjacent and are derived from different HPV types.
- 25 8. The chimeric L1 protein of claim 7 which is comprised from segments from HPV-18 and HPV-45 L1 proteins.
9. The chimeric L1 protein of claim 8 wherein segment 1 contains amino acids 1-265 of HPV-18, segment 2 contains amino acids 265-442 of HPV-45, and segment 3 contains amino acids 443-507 from HPV-18.
- 30 10. A VLP comprising the chimeric HPV L1 protein of claim 1.

11. A vaccine composition comprising the chimeric HPV L1 protein of claim 1.
- 5 12. A therapeutic composition comprising the chimeric HPV L1 protein of claim 1.
13. A gene encoding the chimeric HPV L1 protein of claim 1.
- 10 14. The gene of claim 13, wherein said gene comprises coding sequences of both HPV-18 and HPV-45.
- 15 15. The gene of claim 14, wherein said gene comprises at least the nucleotides of the native HPV-18 L1 gene which encode the R5 epitope.
- 16 16. The gene of claim 15 comprising at least about the N' terminus half of the native HPV-18 L1 gene.
- 20 17. The gene of claim 16, comprising the native HPV-18 L1 gene wherein nucleotides 624 to 1327 have been replaced by the corresponding nucleotides of HPV-45.
18. A baculovirus vector comprising the gene of claim 13.
- 25 19. The VLP of claim 10, wherein said VLP is capable of eliciting antiserum that neutralizes at least two HPV types at a dilution of 1:1000.
20. The VLP of claim 19, wherein said VLP is capable of eliciting antiserum that neutralizes at least two HPV types at a dilution of 1:10,000.
- 30 21. A method for inducing a high titer neutralizing antibody response or cell-mediated immune response against at least two HPV types comprising administering a single type of chimeric HPV L1 protein.

22. The method of claim 21 wherein the antiserum generated by said administration neutralizes said at least two HPV types at a dilution of at least 1:1000.
- 5 23. The method of claim 22 wherein the antiserum generated by said administration neutralizes said at least two HPV types at a dilution of at least 1:10,000.
24. Antisera generated by the method of claim 21.
- 10 25. A method for inducing a high titer neutralizing antibody response or cell-mediated immune response against at least two HPV types comprising administering a VLP comprising a single type of chimeric HPV L1 protein.
- 15 26. The method of claim 25 wherein the antiserum generated by said administration neutralizes said at least two HPV types at a dilution of at least 1:1000.
27. The method of claim 26 wherein the antiserum generated by said administration neutralizes said at least two HPV types at a dilution of at least 1:10,000.
- 20 28. Antisera generated by the method of claim 25.
29. A method for inducing a high titer neutralizing antibody response or cell-mediated immune response against at least three HPV types comprising administering a VLP comprising at least two types of chimeric HPV L1 proteins.
- 25 30. The method of claim 29 wherein the antiserum generated by said administration neutralizes said at least three HPV types at a dilution of at least 1:1000.
- 30 31. The method of claim 30 wherein the antiserum generated by said administration neutralizes said at least three HPV types at a dilution of at least 1:10,000.

32. Antisera generated by the method of claim 29.

33. The method of claim 21, wherein said at least two types of VLPs are
5 HPV-18 and HPV-45.

34. The method of claim 25, wherein said at least two types of VLPs are
HPV-18 and HPV-45.

10 35. The method of claim 29, wherein two of said at least three VLPs are
HPV-18 and HPV-45.

36. A method of vaccinating a subject against at least two types of HPV
comprising administering a vaccine composition comprising at least one correctly
15 folded chimeric HPV L1 protein, wherein said at least one chimeric HPV L1 protein
comprises neutralizing epitopes for at least two HPV types.

37. The method of claim 36, wherein said at least two HPV types are
selected from the group consisting of HPV-6, -11, -16, -18, -31, -33, -35, -39, and -45.
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38. The method of claim 37, wherein said HPV types are HPV-18 and
HPV-45.

39. The method of claim 38 wherein said vaccine composition displays at
25 least the R5 epitope of HPV-18.

40. The method of claim 39 wherein said vaccine composition displays at
least amino acids 53-194 of HPV-18.

30 41. The method of claim 40 wherein said vaccine composition displays at
least the N' terminus half (approximately amino acids 1-194) of HPV-18.

42. The method of claim 36, wherein said vaccine composition comprises a tribrid type of chimeric L1 molecule wherein segments 1 and 2 are adjacent but are derived from different HPV types, and segments 2 and 3 are adjacent but are derived from different HPV types.

43. The method of claim 42 wherein said vaccine composition displays a chimeric L1 containing amino acids 1-265 of HPV-18, followed by amino acids 265-442 of HPV-45, and ending with amino acids 443-507 from HPV-18.

44. The method of vaccination of claim 36, wherein said at least one chimeric L1 protein is expressed on the surface of a VLP.

45. A method of treating a papillomavirus infection characterized by more than one HPV type comprising administering a therapeutic composition comprising HPV VLPs displaying at least one chimeric L1 proteins.

46. A method of treating a papillomavirus infection caused by a first HPV type, concurrently with prophylactically treating at least one other type of HPV infection comprising administering a therapeutic composition comprising HPV VLPs displaying at least one chimeric L1 protein.

47. A method of making a multi-HPV type vaccine or therapeutic composition comprising

- (a) ligating together portions of the native L1 genes encoding for the different epitopes;
- (b) cloning the ligated gene portions into an expression vector;
- (c) expressing the vector in a cell line which allows the formation of VLPs, wherein said VLPs display at least one L1 neutralizing epitope from at least two different HPV types.

48. The method of claim 47 wherein PCR is used to create compatible overhangs on the ends of L1 gene portions to permit ligation of gene portions following restriction endonuclease digestion.

49. The method of claim 47 further comprising disassembly and reassembly of the VLP to permit incorporation of a therapeutic agent or diagnostic agent.

50. A method of diagnosing prior or current papillomavirus infection comprising

- (a) isolating serum from a patient suspected of having a prior or current papillomavirus infection;
- (b) exposing an immobilized chimeric HPV L1 protein to said serum as to allow binding interaction between the HPV L1 epitopes and the antiserum while at the same time separately exposing the identical chimeric HPV L1 to an irrelevant antibody;
- (c) washing said immobilized chimeric HPV L1 such that unbound components are separated;
- (d) exposing said chimeric HPV L1 protein to a labeled reagent that binds with specificity to immunoglobulins of said patient; and
- (e) comparing the amount of label bound to each chimeric HPV L1 sample.

51. The method of claim 50, wherein said chimeric HPV L1 proteins are immobilized on VLPs.

52. The method of claim 51 wherein said chimeric VLPs are immobilized on beads, the surface of a tissue culture dish or cells.

53. The method of claim 50 wherein the presence of antibodies specific for at least two different HPV types are screened for simultaneously using two different labeled reagents.

54. The method of claim 50 where said at least two virus types are HPV-18 and HPV-45.